THE DIAZO AND UROCHROMOGEN REACTIONS IN PULMONARY TUBERCULOSIS *

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This investigation of the diazo and urochromogen reactions in pulmonary tuberculosis was suggested mainly by an article in which Schäffle[1] pointed out, as significant features of his examination, the "difference in mortality percentages between the positive and negative cases and particularly the high death rate among those with a negative diazo and positive urochromogen test."

Schäffle also referred to the original work of Weiss, who, after seven years of investigation, confirmed the observations of Koch that death invariably followed the persistent presence of the diazo reaction in the urine of the tuberculous. Weiss also refers to the frequent disappearance of the diazo reaction shortly before death in tuberculous cases.

The investigation of these reactions was further instigated by the statement of Webster,[2] that "the presence of urochromogen is a contraindication to the tuberculin treatment in tuberculous conditions."

The investigation, therefore, had a twofold purpose: (1) to discover, if possible, the value of the diazo and urochromogen reactions in the prognosis of pulmonary tuberculosis, and (2) to determine whether or not the presence of one or both of these reactions afforded a reliable indication for or against tuberculin treatment in this disease.

The investigation covers 146 cases of pulmonary tuberculosis; the results obtained with reference to the diazo and urochromogen tests are given in Table 1.

Of the 146 cases examined, only one examination was made in forty-two cases, owing to death occurring shortly or other preventing cause.

Successive examinations were made in 104 cases, these 104 cases giving the results shown in Table 2.

Of the twenty-nine cases successively examined showing originally a negative diazo and negative urochromogen (which for clearness I shall call normal) reaction, fourteen showed a later change, and in all these instances this change was to a diazo negative and urochromogen positive. Of this fourteen, eight improved, five were progressive and one patient died (Table 3). Of the seven patients showing a positive reaction to both tests originally, a change was noted in none and all died.

Of the ten patients showing a positive diazo and negative urochromogen originally, six changed. Two changed to normal; one, in a day or two, showing a second change to a negative diazo and positive urochromogen (a reversal of the original reaction) and improved. The other remained normal, and died in a few days.

The remaining four were followed at once by a diazo negative and urochromogen positive (a reversal of the original reaction) and two of the four improved, although one showed a versatility in the art of changing, this diazo negative and urochromogen positive being succeeded first by normal and later by a diazo negative and urochromogen positive.

One of the remaining two was followed by normal and progressed; the other by a positive diazo and negative urochromogen (the original reaction) and died.

TABLE 1.—RESULTS OF INVESTIGATION

Reactions	Total No.	Improved No.	Improved Per Cent.	Progressed No.	Progressed Per Cent.	Died No.	Died Per Cent.
Both negative	38	27	71	7	18.4	4	10.6
Both positive	7	..	....	..	....	7	100
Diazo +, urochromogen —	23	5	25.7	6	26.1	12	48.2
Diazo —, urochromogen +	78	62	79.5	12	15.4	4	5.1

TABLE 2.—RESULTS OF SUCCESSIVE EXAMINATIONS IN 104 CASES

Reactions	Total No.	Improved No.	Improved Per Cent.	Progressed No.	Progressed Per Cent.	Died No.	Died Per Cent.
Both negative	29	21	72.4	6	20.7	2	6.9
Both positive	7	..	....	..	....	7	100
Diazo +, urochromogen —	10	4	40	3	30.3	3	30.3
Diazo —, urochromogen +	58	45	76	11	19	2	5

TABLE 3.—CHANGES IN REACTION

Reaction: Original	No.	Change	No.	Improved	Progressed	Died
D —, U —	29	D —, U +	14	8	5	1
D +, U +	7			..	..	7
D +, U —	10	D —, U —	2	1*	..	1
		D —, U +	4	2†	1‡	1§
D —, U +	58	D —, U —	20	18	..	2
		D +, U —	2	..	1	1

* Followed by D —, U +.
† One patient changed to normal and later to D —, U +.
‡ Followed by normal.
§ Followed by D +, U — (original reaction).

* Read before the Hawaiian Territorial Medical Society, Nov. 6, 1915.

1. Schäffle, Karl: A Comparison Between the Urochromogen and Diazo Tests in the Prognosis of Tuberculosis, THE JOURNAL A. M. A., Oct. 10, 1914, p. 1294.

2. Webster, R. W.: Diagnostic Methods, Chemical, Bacteriological and Microscopical, Ed. 4, Philadelphia, P. Blakiston's Son & Co., 1914, p. 245.

Of the fifty-eight cases showing originally a negative diazo and positive urochromogen, twenty-two cases showed a change in reaction.

Of these twenty-two, twenty were to normal (negative to both tests) of which eighteen improved and two patients died. The remaining two cases showed a reversal to a diazo positive and urochromogen negative; one progressed and one patient died (Table 3).

So far as prognosis is concerned, therefore, my results do not agree with those of the authors quoted above. The results disagree in two important particulars:

1. I have not found a particularly high death rate among those patients showing a negative diazo and positive urochromogen. On the contrary, from 76 to 79 per cent. of patients showing this reaction have improved.

2. I have not found any case in which the diazo and urochromogen tests were both positive in which the diazo disappeared before death. This observation is admittedly of little value, as only seven such cases were observed. On the other hand, when the diazo is present but not the urochromogen reaction, the peculiar fact is observed, from the limited data collected, that in fatal or progressive cases the diazo does here disappear; but should the urochromogen take its place, a favorable prognosis may be ventured.

The second purpose of this examination, to discover the value of the urochromogen reaction as an indication for or against tuberculin treatment, has also resulted in findings contrary to those of the author quoted.

During the year there were admitted to hospital fifty-nine patients with pulmonary tuberculosis with the urochromogen reaction and with the following stadia: L 1 S, 4; L 2 S, 44; L 3 S, 10; L 3 S, 1.

Of this fifty-nine, twenty-three were (according to the temperature and other indications) favorable for and received tuberculin treatment and their stadia were as follows: L 1 S, 4; L 2 S, 19; L 3 S, 0.

The result is given in Table 4.

TABLE 4.—RESULT OF TUBERCULIN TREATMENT IN TWENTY-THREE CASES

Stage	Improved	Progressed	No Change	Died	Total
L 1 S.....	4	0	0	0	4
L 2 S.....	15	1	3	0	19

Of the nineteen cases in which there has been improvement, the urochromogen reaction has disappeared in seven and will probably disappear in others as treatment progresses. Thus it would appear that almost 40 per cent. of those treated with tuberculin would not have received such treatment if the urochromogen reaction had been accepted as a contraindication to such treatment, and as 82 per cent. of those with the urochromogen reaction improved markedly under tuberculin treatment, the urochromogen reaction would not appear to be of much value as a contraindication.

On the other hand, the urochromogen reaction appeared in six cases while under treatment; four of these patients improved and in two there was no change or progression. An interesting fact in regard to the last two is the fact that tuberculin treatment was stopped some time before the appearance of the urochromogen reaction, the inference being, in these cases, that other factors contraindicated tuberculin treatment before the urochromogen reaction.

It has further been observed that patients with a urochromogen reaction may, under tuberculin or other treatment, improve to the extent of presenting the physical signs of a healed lesion and all other indications of an arrested case, and the urochromogen reaction still be positive.

Since the urochromogen reaction is undoubtedly an indication of abnormal metabolism, it may be that no patient can be classified as arrested who still presents the urochromogen reaction. This sign, therefore, may yet prove of value in this connection.

Concerning the diazo reaction as a contraindication to tuberculin treatment, it should suffice to say that while the diazo reaction has never been taken into consideration as a factor in deciding on tuberculin treatment, no patient with tuberculosis noted as having the diazo reaction has been treated with tuberculin.

Although this investigation may seem to have led nowhere, this is not the case, as the following conclusions can be drawn from it:

1. The only favorable change from normal (both tests absent) is to a negative diazo and positive urochromogen.

(This would also mean that at an original examination it is the only favorable deviation from normal.)

2. A change from either negative diazo to either positive diazo is most unfavorable.

3. The appearance of both reactions is of most grave portent. Such patients generally die.

4. When there is a change from a positive diazo and a negative urochromogen, the only favorable one is a reversal (that is, to a negative diazo and positive urochromogen).

When the change is to positive to both tests a fatal issue is prognosticated. On the other hand, a change to normal (contrary to what we would expect) is of very grave prognosis. If the urochromogen reaction does not appear concomitantly with the disappearance of the diazo (or at least in a day or two) the prognosis is of the worst.

5. The disappearance of the diazo reaction (when both tests have been positive) has not been observed as heralding a fatal issue.

6. The disappearance of the diazo may be grave or favorable (a corollary to No. 4)—grave if the urochromogen does not take its place, favorable if it does.

7. The urochromogen reaction is probably of little value as a contraindication to tuberculin treatment, and should it be of any value at all, the probabilities are that other factors show such treatment to be contraindicated better and earlier than the urochromogen reaction.

8. This also applies to the diazo reaction as a contraindication to treatment.

9. Should the urochromogen reaction eventually prove of any value in the tuberculin treatment, I believe it will be for a diametrically opposed purpose to that referred to (as a contraindication to beginning tuberculin treatment): in other words, its presence may be a valuable contraindication to discontinuing tuberculin treatment in cases to which all other signs point as arrested. On this point I have not sufficient material as yet to say definitely. I can only state that it appears here to be of value, and I hesitate now to discontinue tuberculin in arrested cases which show this reaction.